DECLARATION OF CHRISTOPHER SOMERVILLE UNDER 37 C.F.R. § 1.132

Attorney Docket	2300-1487
First Named Inventor	Williams et al.
Application Number	09/313,292
Filing Date	May 13, 1999
Group Art Unit	1631
Examiner Name	J. Brusca
Title: *Novel Human Genes and Gene Expression Products*	

Dear Sir:

1. I, Christopher R. Somerville, declare and say I am a resident of the State of California. My residence address is 5 Valley Oak, Portola Valley, CA 94028.

2. I hold a B.Sc. degree in Mathematics, which I received from the University of Alberta, Canada in 1974. I further hold M.Sc. and Ph.D. degrees in Genetics, which I received from the University of Alberta, Canada in 1976 and 1978, respectively.

3. I am a Director of the Carnegie Institution of Washington Department of Plant Biology and a Professor of the Department of Biological Sciences at Stanford University. I am an elected member of the U.S. National Academy of Sciences, and an elected fellow of the Royal Societies of London and Canada. I serve on the editorial boards of several international peer-reviewed journals and have served on several panels for the NIH, NSF and USDA. I have worked in the field of recombinant DNA technology for over 20 years and have published over 150 articles in the fields of genetics, biochemistry, molecular biology and genomics (see curriculum vitae attached).

4. I have reviewed the '292 patent application, the first Office Action (specifically section No. 13) mailed December 1, 2000, the final Office Action (specifically section

No. 6) mailed August 31, 2001, and the Advisory Action mailed April 25, 2002 in the '292 application.

5. I understand the inventions at issue (hereinafter "Inventions") are defined by the following claims:

Claims 123-125

Claim 123 is a formula in which the Invention is defined as a genus of polynucleotides characterized as having the common structural feature of a nucleotide sequence containing a minimum of 150 contiguous nucleotides of SEQ ID NO:972. I understand that the genus of polynucleotides defined by Claim 123 includes polynucleotides that contain additional sequences (i.e. flanking sequences) other than the specified contiguous region. Claim 124 defines the Invention as a vector containing the Invention of Claim 123, and Claim 125 defines the Invention as host cells containing the Invention of Claim 124.

Claim 126

Claim 126 is a formula in which the Invention is defined as a genus of polynucleotides characterized by the common structural feature of (1) a length that is a minimum of 200; and (2) sufficiently structural similarity to SEQ ID NO:972 to allow the polynucleotide to hybridize under stringent conditions to a polynucleotide having a sequence of SEQ ID NO:972.

Claim 127

Claim 127 defines the Invention as a genus of polynucleotides characterized as containing a sequence that is the same as the sequence of an insert found in the clone number M00007118B:B04, deposited with the ATCC. I understand that the genus of polynucleotides defined by claim 127 includes polynucleotides that contain additional sequences (i.e. flanking sequences) other than that specified by SEQ ID NO:972.

Claims 128-130

Claim 128 defines the Invention as a genus of isolated polynucleotides characterized as having the common structural feature of a nucleotide sequence containing a minimum of 150 contiguous nucleotides of SEQ ID NO:972, obtained as a product of amplification using at least one oligonucleotide primer that contains at least 15 contiguous nucleotides of the sequence of SEQ ID NO:972. Claim 129 defines the Invention as a vector containing the Invention of Claim 128, and Claim 130 defines the Invention as host cells containing the Invention of Claim 128.

In this Declaration, I will be addressing these Inventions.

6. I have been asked to opine of the following questions:

a) Would one of ordinary skill in the art to which the Inventions pertain (hereinafter the "Skilled Person") would conclude from a review of the '292 application as a whole that the Inventions are described therein and the inventors were in possession of the Inventions?

b) Would the Skilled Person conclude from a review of the '292 application as a whole that the disclosures therein are representative of the genera defined by the Inventions?

It is my opinion, based on the facts and reasoning set forth below, that the answer to each of these questions is "yes."

Skilled Person

7. It is my understanding that the application is to be viewed from the standpoint of one of ordinary skill in the art in the relevant field at the time of filing of the application (referred to here as the "Skilled Person"). The '292 application was filed on May 13, 1999 and relates to the field of recombinant DNA technology. I would expect a Skilled Person in the field of recombinant DNA technology in May 1999 to

have been represented by a scientist with a Ph.D. degree and two years of post-doctoral training. I consider that such a Skilled Person would have the ability to analyze a DNA sequence using the common general knowledge, tools, and methods available in the field and without inventive effort. Furthermore, such a Skilled Person would have had access to and would have used as needed persons of ordinary skill in other technical fields, such as (by way of illustration and not limitation) cellular biology, oncology, biochemistry, immunology, physiology and diagnostics.

8. In May 1999, the common general knowledge, tools, and well-known methods available in this field were extensive. Widely available methods included nucleotide hybridization, nucleic acid cloning, polymerase chain reaction (PCR), reverse transcriptase PCR (RT-PCR), gene sequencing and cDNA library construction and screening. In addition, several "bioinformatics" tools were available, such as bioinformatics programs for searching a database of nucleic acids sequences for similar nucleic acid sequences (e.g. BLAST), programs for comparing two nucleic acid sequence (e.g. the BESTFIT or GAP programs as provided by the University of Wisconsin's GCG program) and programs for predicting and annotating coding sequences of genes (e.g. GENSCAN and XGRAIL).

9. Since I a) regularly attended external and internal meetings on molecular biology topics at which Skilled Persons presented their research, b) regularly read and reviewed scientific literature in which Skilled Persons presented their research, and c) was head of a laboratory in which several Skilled Persons have received training, prior to and during May, 1999, I believe that I am qualified by training and experience to address what a Skilled Person would have understood from a reading of the specification of U.S. Patent Application No. 09/313,292, as of its filing date on May 13, 1999.

10. The following remarks constitute the basis for my opinion that the Skilled Person would conclude, from a review of the '292 application as a whole, that the Inventions were described in the '292 application and in the inventors' possession, and further that the disclosure of '292 application contains representative examples of the Inventions.

Claims 123-125

11. The specification describes the Inventions of Claims 123-125 in a number of passages, including the following:

In the sequence listing submitted as part of the application, SEQ ID NO:972 is provided as follows:

<400> 972
aattccgttg ctgtcggaga gactgaaaac agagaaaaag ttgccgcctc accaaaaagt 60
cccactgctg cactcaatga aagcctggtg gaatgtccca agtgcaatat acagtatcca 120
gccactgagc atcgcgatct gcttgtccat gtggaatact gttcaaagta gcaaaataag 180
tatttgtttt gatattaaaa gattcaatac tgtatttttct gttagcttgt gggcattttg 240
aattatatat ttcacatttt gcataaaact gcctatctac ctttgacact ccagcatgct 300

An actual clone encompassing the sequence of SEQ ID NO:972 was deposited with the A.T.C.C. as clone number M00007118B:B04 of ATCC Deposit Number PTA-60.

On page 4, line 34 to page 5, line 6 of the specification, particular lengths of regions of SEQ ID NO:972 are described:

> Isolated polynucleotides and polynucleotide fragments of the invention comprise at least about 10, about 15, about 20, about 35, about 50, about 100, about 150 to about 200, about 250 to about 300, or about 350 contiguous nt selected from the polynucleotide sequences as shown in SEQ ID NOS:1-2707.

Taking these disclosures together, the Skilled Person would find described in the '292 application all sequences of at least 150 contiguous polynucleotides contained within SEQ ID NO:972.

12. I am informed that in the language of patent law the term "comprise" as used in the above claims means that flanking sequences can be present in addition to the specified sequence. A genus of polynucleotides containing flanking regions is describe in the '292 application, as discussed further below.

13. Nucleic acid probes containing the specified sequence, which a Skilled Person would recognize as often longer than the specified sequence from the SEQ ID, are described in several positions in the specification, for example:

on page 5, lines 7-14:

> Probes specific to the polynucleotides of the invention can be generated using the polynucleotide sequences disclosed in SEQ ID NOS:1-2707. The probes are preferably at least about a 12, 15, 16, 18, 20, 22, 24, or 25 nt fragment of a corresponding contiguous sequence of SEQ ID NOS:1-2707, and can be less than 2, 1, 0.5, 0.1, or 0.05 kb in length. The probes can be synthesized chemically or can be generated from longer polynucleotides using restriction enzymes. The probes can be labeled, for example, with a radioactive, biotinylated, or fluorescent tag. Preferably, probes are designed based upon an identifying sequence of a polynucleotide of one of SEQ ID NOS:1-2707 .

and on page 5, line 34 to page 6, line 5:

> The subject nucleic acid compositions can be used to, for example, produce polypeptides, as probes for the detection of mRNA of the invention in biological samples (e.g., extracts of human cells) to generate additional copies of the polynucleotides, to generate ribozymes or antisense oligonucleotides, and as single stranded DNA probes or as triple-strand forming oligonucleotides. The probes described herein can be used to, for example, determine the presence or absence of the polynucleotide sequences as shown in SEQ ID NOS:1-2707 or variants thereof in a sample. These and other uses are described in more detail below.

Furthermore, Sambrook et al., *Molecular Cloning: A Laboratory Manual*, 2nd Ed., (1989) Cold Spring Harbor Press, Cold Spring Harbor, NY., which is incorporated by reference into the application, discloses several types of probes that contain flanking sequences, including hybridization probes, oligonucleotide probes, RNA probes, plasmid probes and polymerase chain reaction probes. For example, a Skilled Person would recognize that a probe may contain polylinker sequences, or an oligonucleotide "tail". The Skilled Person would also know that much longer sequences, such as vectors containing the sequence specified from the SEQ ID can be used as probes.

14. Vectors containing the specified sequence, which a Skilled Person would recognize as always being longer than the specified sequence, are described in several positions in the specification. For example, on page 5, lines 19-24, that an Invention can be contained in a vector is recited:

> The polynucleotides of the invention can be provided as a linear molecule or within a circular molecule, and can be provided within autonomously replicating molecules (vectors) or within molecules without replication sequences. Expression of the polynucleotides can be regulated by their own or by other regulatory sequences known in the art.

On page 9, lines 14-30, several types of vector, including expression vectors, viral vectors, non-viral vectors and plasmids are described:

> Appropriate polynucleotide constructs are purified using standard recombinant DNA techniques as described in, for example, Sambrook *et al.*, *Molecular Cloning: A Laboratory Manual, 2nd Ed.*, (1989) Cold Spring Harbor Press, Cold Spring Harbor, NY, and under current regulations described in United States Dept. of HHS, National Institute of Health (NIH) Guidelines for Recombinant DNA Research. The gene product encoded by a polynucleotide of the invention is expressed in any expression system, including, for example, bacterial, yeast, insect, amphibian and mammalian systems. Vectors, host cells and methods for obtaining expression in same are well known in the art. Suitable vectors and host cells are described in USPN 5,654,173.

> Polynucleotide molecules comprising a polynucleotide sequence provided herein are generally propagated by placing the molecule in a vector. Viral and non-viral vectors are used, including plasmids. The choice of plasmid will depend on the type of cell in which propagation is desired and the purpose of propagation. Certain vectors are useful for amplifying and making large amounts of the desired DNA sequence. Other vectors are suitable for expression in cells in culture. Still other vectors are suitable for transfer and expression in cells in a whole animal or person. The choice of appropriate vector is well within the skill of the art. Many such vectors are available commercially. Methods for preparation of vectors comprising a desired sequence are well known in the art.

and further examples of types of vectors that may encompass a polynucleotide of the invention may be found on page 42, line 32-page 43 line 5.

> Viral-based vectors for delivery of a desired polynucleotide and expression in a desired cell are well known in the art. Exemplary viral-based vehicles include, but are not limited to, recombinant retroviruses (see, e.g., WO 90/07936; WO 94/03622; WO 93/25698; WO 93/25234; USPN 5,219,740; WO 93/11230; WO 93/10218; USPN 4,777,127; GB Patent No. 2,200,651; EP 0 345 242; and WO 91/02805), alphavirus-based vectors (e.g., Sindbis virus vectors, Semliki forest virus (ATCC VR-67; ATCC VR-1247), Ross River virus (ATCC VR-373; ATCC VR-1246) and Venezuelan equine encephalitis virus (ATCC VR-923; ATCC VR-1250; ATCC VR 1249; ATCC VR-532), and adeno-associated virus (AAV) vectors (see, e.g., WO 94/12649, WO 93/03769; WO 93/19191; WO 94/28938; WO 95/11984 and WO 95/00655).

15. On page 4 lines 16-20 of the specification, cDNA polynucleotides containing the specified sequence, which a Skilled Person would recognize as longer than the specified sequence, are described:

> The term "cDNA" as used herein is intended to include all nucleic acids that share the arrangement of sequence elements found in native mature mRNA species, where sequence elements are exons and 3' and 5' non-coding regions. Normally mRNA species have contiguous exons, with the intervening introns, when present, being removed by nuclear RNA splicing, to create a continuous open reading frame encoding a polypeptide of the invention.

Furthermore, the actual vector encompassing the sequence of SEQ ID NO:972 was deposited with the A.T.C.C. is a cDNA clone.

16. Finally, on page 4, lines 13-30, the specification discloses a gene containing the specified sequence, which a Skilled Person would recognize as longer than the specified sequence, is described:

> The subject nucleic acids can be cDNAs or genomic DNAs, as well as fragments thereof, particularly fragments that encode a biologically active gene product .....
>
> A genomic sequence of interest comprises the nucleic acid present between the initiation codon and the stop codon, as defined in the listed sequences, including all of the introns that are normally present in a native chromosome. It can further include the 3` and 5` untranslated regions found in the mature mRNA. It can further include specific transcriptional and translational regulatory sequences, such as promoters, enhancers, etc., including about 1 kb, but possibly more, of flanking genomic DNA at either the 5` and 3` end of the transcribed region. The genomic DNA can be isolated as a fragment of 100 kbp or smaller; and substantially free of flanking chromosomal sequence. The genomic DNA flanking the coding region, either 3` and 5`, or internal regulatory sequences as sometimes found in introns, contains sequences required for proper tissue, stage-specific, or disease-state specific expression.

17. In summary, the '292 specification specifically describes the sequence of SEQ ID NO:972 and the '292 specification specifically describes polynucleotides containing at least 150 contiguous nucleotides of SEQ ID NO:972. The '292 specification also specifically describes a wide variety of polynucleotides containing at least 150 contiguous nucleotides of SEQ ID NO:972 along with flanking sequences, e.g. probes, vectors, cDNAs, clones, full length cDNAs, genes etc. As such the '292 specification describes large polynucleotides containing fragments of SEQ ID NO:972 that are, for example, useful as probes or starting materials for probes (see, e.g., page 5, lines 7-14 of the '292 specification). The vector containing a cDNA containing the sequence of SEQ ID NO:972 and deposited with the A.T.C.C. is an example of a polynucleotide containing SEQ ID NO:972 and having such flanking sequences. The overall disclosure of the specification demonstrates that there is no criticality to sequences flanking the polynucleotides of the Invention. Rather, selection of such

flanking sequences is an arbitrary matter of design. The Skilled Person would readily appreciate from the specification that the sequence of SEQ ID NO:972 can be incorporated within a vast number of larger polynucleotides, and that each of these sequences is identifiable as having at least 150 contiguous nucleotides of SEQ ID NO:972.

18. When read in conjunction with the '292 specification, it is my unequivocal opinion that, a Skilled Person would find that the '292 specification describes polynucleotides fully representative of the genus of polynucleotides of the Invention since

a) the Skilled Person would recognize disclosure of SEQ ID NO:972 as fully representative of the genus of the Invention since it is a complete disclosure of the common structural feature (i.e., at least 150 contiguous nucleotides of SEQ ID NO:972) of the Inventions; and

b) the Skilled Person would recognize the vector containing a cDNA containing the sequence of SEQ ID NO:972 and deposited with the A.T.C.C. is an example of a polynucleotide containing SEQ ID NO:972 having flanking sequences and as being fully representative of large polynucleotides that can serve as probes or starting materials for probes in cancer diagnostics.

19. Based upon the above, the Skilled Person would conclude that the specification substantially and in detail describes the genus of polynucleotides encompassed in these claims 123-125. It is therefore my unequivocal opinion that a Skilled Person would, in May 1999, thus would find a clear and unambiguous description of the Inventions in Claims 123-125. Based on the foregoing, it is also my unequivocal opinion that a Skilled Person would find that the '292 specification demonstrates that applicants had possession of the genera of polynucleotides of claims 123-125.

20. Furthermore, a Skilled Person, by performing a simple sequence comparison, e.g. a pairwise "BESTFIT" alignment between SEQ ID NO:972 and any given nucleotide would have been able to straightforwardly determine whether a given polynucleotide fell within any one of the claims: the given polynucleotide either has 150 nucleotides of sequence identity with SEQ ID NO:972 or it does not.

Claim 126

21. I shall now address the Invention of Claim 126. In addition to the above-described portions of the specification and information known to the Skilled Person, I rely on the following in forming my opinion. .

22. Page 2 line 34 to page 3, line 5 of the specification describes a genus of polynucleotides that hybridize under stringent conditions to a polynucleotide having a sequence provided by the sequence listing:

> The polynucleotides of the invention also include polynucleotides having sequence similarity or sequence identity. Nucleic acids having sequence similarity are detected by hybridization under low stringency conditions, for example, at 50°C and 10XSSC (0.9 M saline/0.09 M sodium citrate) and remain bound when subjected to washing at 55°C in 1XSSC. Sequence identity can be determined by hybridization under stringent conditions, for example, at 50°C or higher and 0.1XSSC (9 mM saline/0.9 mM sodium citrate). Hybridization methods and conditions are well known in the art, see, *e.g.*, USPN 5,707,829.

23. The specification, on page 3, lines 5 to 19, further describes that the Inventions may be allelic variants, cDNAs or genes, and may be from a variety of species, including humans.

> Nucleic acids that are substantially identical to the provided polynucleotide sequences, *e.g.* allelic variants, genetically altered versions of the gene, *etc.*, bind to the provided polynucleotide sequences (SEQ ID NOS:1-2707) under stringent hybridization conditions. By using probes, particularly labeled probes of DNA sequences, one can isolate homologous or related genes. The source of homologous genes can be any species, *e.g.* primate species,

> particularly human; rodents, such as rats and mice; canines, felines, bovines, ovines, equines, yeast, nematodes, *etc.*
>
> Preferably, hybridization is performed using at least 15 contiguous nucleotides (nt) of at least one of SEQ ID NOS:1-2707. That is, when at least 15 contiguous nt of one of the disclosed SEQ ID NOS. is used as a probe, the probe will preferentially hybridize with a nucleic acid comprising the complementary sequence, allowing the identification and retrieval of the nucleic acids that uniquely hybridize to the selected probe. Probes from more than one SEQ ID NO. can hybridize with the same nucleic acid if the cDNA from which they were derived corresponds to one mRNA. Probes of more than 15 nt can be used, e.g., probes of from about 18 nt to about 100 nt, but 15 nt represents sufficient sequence for unique identification.

24. It is well established that, in order to hybridize, two polynucleotides must share a definable structural characteristic: a region of significant sequence identity. The structural characteristic that defines the claimed genus is SEQ ID NO:972, to which members of the group hybridize under stringent conditions. Some of the polynucleotides encompassed by the claim may be longer than the sequence of SEQ ID NO:972 and contain flanking sequences, however, since they must be able to hybridize with a specified polynucleotide they must have sequences that are similar to the sequence of the specified polynucleotide, and thus are limited in structure by this requirement. As such, the structural characteristic defining this genus of claimed sequences is the sequence of SEQ ID NO:972.

25. I have also reviewed the U.S. Patent & Trademark Office's "Synopsis of Application of Written Description Guidelines,", as posted to the U.S.P.T.O world wide website on March 1, 200 and I agree with the assertion that "a person of skill in the art would not expect substantial variation among species encompassed within the scope of the claim because the highly stringent hybridization conditions set forth in the claim yield structurally similar DNAs", as recited on page 36. I also agree with the Synopsis of Application of Written Description Guidelines in that a recitation of "hybridization" in a claim imposes a structural limitation onto the claimed Inventions.

26. It is therefore my unequivocal opinion that a Skilled Person would, in May 1999, have found the specific description of the claimed genus of polynucleotides in the specification to be a sufficient structural description of the claimed Inventions and to demonstrate applicants had possession of the Invention of Claim 126.

27. Furthermore, the Skilled Person would have been able to straightforwardly determine whether a given polynucleotide falls within Claim 126 by performing a straightforward stringent hybridization experiment, or by calculating the Tm of the a hybrid polynucleotide molecule under certain hybridization conditions using the well known equation provided by Sambrook et al (Molecular Cloning: A Laboratory Manual, CSHL Press, 1989).

"Tm = 81.5 + 1.6(log10[Na+]) + 0.41(fraction G + C)
– 0.63(% formamide) – (600/length of probe)"

Claim 127

28. I will now discuss the Invention of Claim 127. In addition to the above-described portions of the specification and information known to the Skilled Person, I rely on the following in forming my opinion.

29. Table 1 of the '292 application describes biological deposits which include vectors containing an insert, which insert contains the sequences described in the application. Table 1 indicates that a clone encompassing the sequence of SEQ ID NO:972 is deposited as clone M00007118B:B04 of Deposit Number PTA-60 at the ATCC.

30. SEQ ID NO:972 represents a part of the nucleotide sequence contained within the insert of the deposited clone, and, as such, the deposited clone contains an polynucleotide insert that is longer than SEQ ID NO:972 and contains flanking sequences. Since the deposited clone is from a library made from mRNA, the flanking sequence are cDNA flanking sequences.

31. Based upon the above disclosures in the '292 application, it is my unequivocal opinion that a Skilled Person would find that the '292 application describes the Invention of Claim 127 and recognize that the inventors were in possession of that Invention.

Claims 128-130

32. I will now discuss the Invention of Claims 128-130. In addition to the above-described portions of the specification and other information known to the Skilled Person, I rely on the following in forming my opinion.

33. Amplification is a process for synthesizing a nucleic acid enzymatically. To perform amplification, at least one oligonucleotide probe (i.e. a primer of a defined sequence) hybridizes with (i.e. base pairs to) a template nucleic acid (i.e., the starting material), and the probe is enzymatically extended to form a copy of one strand of the nucleic acid. Subsequent extension steps amplify both strands of the nucleic acid to form a duplex nucleic acid product that contains at least the probe binding site. Probe binding sites are usually at least 12-15 nucleic acids in length, and, as such, both the amplification product and the probes share a sequence of at least 12-15 nucleotides.

34. Amplification strategies, such as the polymerase chain reaction (PCR), lockdown PCR, and rapid amplification of cDNA ends (RACE) were well understood and practiced a Skilled Person in 1999 (e.g. as described by the laboratory manuals Ausubel et al. (*Short Protocols in Molecular Biology*, 3rd ed., Wiley & Sons, 1995 and Sambrook et al., (*Molecular Cloning: A Laboratory Manual*, Second Edition, 1989 Cold Spring Harbor, N.Y.). In many amplification strategies, such as RACE and lockdown PCR, nucleotide sequences flanking a sequence of interest may be amplified. In the specification, several amplification strategies are detailed, such as PCR, lockdown PCR and RACE. In most PCR methods, probes are first designed,

and the PCR is performed. The specification provides description of a SEQ ID NO:972, a description of probes, and a description of PCR methods as follows:

35. SEQ ID NO:972 is described in the sequence listing submitted as part of the application, as recited in paragraph 11, *supra*.

36. Probe sequences are detailed in the specification on page 5, lines 7-10:

> Probes specific to the polynucleotides of the invention can be generated using the polynucleotide sequences disclosed in SEQ ID NOS:1-2707. The probes are preferably at least about a 12, 15, 16, 18, 20, 22, 24, or 25 nt fragment of a corresponding contiguous sequence of SEQ ID NOS:1-2707,

37. Polymerase Chain Reaction (PCR) is detailed in the specification at page 23, lines 4-8.

> Alternatively, the Polymerase Chain Reaction (PCR) is another means for detecting small amounts of target nucleic acids (see, *e.g.*, Mullis *et al.*, *Meth. Enzymol.* (1987) *155*:335; USPN 4,683,195; and USPN 4,683,202). Two primer polynucleotides nucleotides that hybridize with the target nucleic acids are used to prime the reaction. The primers can be composed of sequence within or 3' and 5' to the polynucleotides of the Sequence Listing

38. On page 7, lines 1-11, RACE is described:

> "Rapid amplification of cDNA ends," or RACE, is a PCR method of amplifying cDNAs from a number of different RNAs. The cDNAs are ligated to an oligonucleotide linker, and amplified by PCR using two primers. One primer is based on sequence from the instant polynucleotides, for which full length sequence is desired, and a second primer comprises sequence that hybridizes to the oligonucleotide linker to amplify the cDNA. A description of this methods is reported in WO 97/19110. In preferred embodiments of RACE, a common primer is designed to anneal to an arbitrary adaptor sequence ligated to cDNA ends (Apte and Siebert, Biotechniques (1993) 15:890-893; Edwards et al., Nuc. Acids Res. (1991) 19:5227-5232). When a single gene-specific RACE primer is paired with the common primer, preferential amplification of sequences between the single gene specific primer and the common primer occurs. Commercial cDNA pools modified for use in RACE are available.

39. On page 7, lines 12-16, lockdown PCR is described:

> Another PCR-based method generates full-length cDNA library with anchored ends without needing specific knowledge of the cDNA sequence. The method uses lock-docking primers (I-VI), where one primer, poly TV (I-III) locks over the polyA tail of eukaryotic mRNA producing first strand synthesis and a second primer, polyGH (IV-VI) locks onto the polyC tail added by terminal deoxynucleotidyl transferase (TdT)(see, e.g., WO 96/40998).

40. In summary, the specification specifically describes SEQ ID NO:972, the specification specifically describes that oligonucleotide probes for use in amplification can be at least 15 contiguous nucleotides of an SEQ ID NO:972, and the specification specifically describes starting material for use in the amplification process, as well as the polynucleotides that would be produced by amplification using the probes and the starting material. These polynucleotides share the structural feature of at least 150 contiguous nucleotides of SEQ ID NO:972.

41. Based upon the above disclosures in the '292 application, it is my unequivocal opinion that a Skilled Person would find that the '292 application describes the Invention of Claims 128-130 and recognize that the inventors were in possession of that Invention

The Office Actions

42. I have been asked to comment on the Office Actions, including the first Office Action (specifically section No. 13) mailed December 1, 2000 and the final Office Action (specifically section No. 6) mailed August 31, 2001.

43. It is my understanding that the positions outlined in these Office Actions were taken with respect to other claimed Inventions, and that the same reasoning might be applied to the new claims directed to these Inventions.

44. As I understand it, claims directed to the above-described Inventions have been rejected as containing subject matter which was not described in the specification in such a way as to reasonably convey to one of ordinary skill in the art that the Inventors, at the time the application was filed, had possession of the claimed invention. Specifically, the Office Action argues that the specification provides insufficient written description to support the genus of nucleic acid sequences encompassed by the claims, which include sequences longer than SEQ ID NO:972 and sequences that hybridize to SEQ ID NO:972. The Office Actions further asserts that with the exception of a polynucleotide that is limited to at least 150 contiguous nucleotides of SEQ ID NO:972 and no more, one of ordinary skill in the art cannot envision the detailed chemical structure of the encompassed polynucleotides, regardless of the complexity or simplicity of the method of isolation. Based on my knowledge of the Skilled Person, I disagree with this statement.

45. As I have discussed above, the sequence of SEQ ID NO:972 defines structural features commonly possessed by members of each of the genera of the Inventions that distinguish them from other polynucleotides. SEQ ID NO:972 thus defines the claimed genera of polynucleotides such that a Skilled Person would have recognized that the inventors had possession of and had invented the claimed polynucleotides. Moreover, the Skilled Person would have been able to straightforwardly determine whether a given polynucleotide falls within any one of the claims based on the provided structural characteristics or routine hybridization experiments. Only routine methodologies would be required to determine whether a given polynucleotide would be within a genus of an Invention. The specification provides, therefore, sufficient written description of the characterizing details sufficient to distinguish the claimed genera of polynucleotides from all others, which means the genera are readily recognizable by the Skilled Person.

46. Furthermore, in reviewing the Office Actions, I note that the written description rejection cites the following court decisions in support of the rejection: *Amgen, Inc. v. Chugai Pharmaceutical Co.*, *Fiers v. Revel*, *Fiddes v. Baird*, and *University of California v. Eli Lilly and Co.* I understand that the disputed patent applications were filed in the between the late 1970's and the mid-1980s.

47. Since the field of recombinant DNA technology is a rapidly evolving, and most major technological advances have been made in the last 20 years (e.g. computer programs for comparing nucleic acids), a Skilled Person had a dramatically higher skill level in May 1999 as compared to the filing dates of the applications involved in the above court decisions. As I understand it, the written description requirement is evaluated in the context of the person of ordinary skill in the art at the time of filing. Because of the advances in the art, I do not believe that a statement regarding what one of ordinary skill can or cannot do in the above cases could be evidence with respect to what the Skilled Person in May of 1999 could or could not do.

48. I, Christopher R. Somerville, hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title XVIII of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

9/27/02
Date

Christopher R. Somerville, Ph.D.

CURRICULUM VITAE

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Home: 5 Valley Oak, Portola Valley, CA 94028

Birthdate: October 11, 1947

Citizenship: USA (Naturalized 2/28/95)

Education:

Ph.D. (genetics), 1978, University of Alberta, *E. coli* mutants defective in pppGpp hydrolysis
M.Sc. (genetics), 1976, University of Alberta, Positive gene regulation by *relA* in *E. coli*
B.Sc. (mathematics), 1974, University of Alberta

Employment:

Director, Carnegie Institution of Washington Department of Plant Biology, 1994-
Professor, Department of Biological Sciences, Stanford University, 1994-
Professor, Department of Botany and Plant Pathology and MSU-DOE Plant Research Laboratory, Michigan State University, 1986-93
Associate Professor, MSU-DOE Plant Research laboratory, Michigan State University, 1982-86
Assistant Professor, Department of Genetics, University of Alberta, 1981 -82
Research Associate, Department of Agronomy, University of Illinois 1978-81

Awards:

Kuhmo Award (2001); D.Sc., Wageningen University (1998);
Visiting Professor, University of Glasgow (1998-);
D.Sc., University of Alberta (1997);
Elected to U.S. National Academy of Sciences (1996);
D.Sc., Queens University (1993);
American Society of Plant Physiologists Gibbs Medal (1993);
Elected Fellow of Royal Society of Canada (1993);
Humbolt Senior Research Award (1992);
MSU Distinguished Faculty Award (1992);
Elected Fellow of Royal Society London (1991);
Schull Award, American Society of Plant Physiologists (1987);

National Science Foundation Young Presidential Investigator Award (1984)

Professional Service:
Panel Member, USDA-ARS Federal Support for Soybean Research, (1981); Panel Member, USDA-CRGO Photosynthesis Panel, Washington, (1983-84); Editorial Committee, Photosynthesis Research (1984-87); Editorial Committee, Plant Physiology (1985-91); American Society of Plant Physiologists, Futures Committee (1985-86); Panel Member, NSF Postdoctoral fellowships in Plant Biology (1985); Panel Member, NSF Eukaryotic Genetics Panel (1985-88); Panel Member, NIH Molecular Biology Panel (1989); Editorial Committee, Archives Biochem. Biophys. (1986-); Panel Member, NSF Presidential Investigator Panel (1986); Editorial Committee, Development (1986-93); Editorial Committee, Developmental Genetics (1989-91); American Society Plant Physiologists Publication Committee (1989-91); Member, Arabidopsis Genome Project Steering Committee (1989-94); Panel Member, USDA Genome Project Steering Committee (1989-93); Program Manager, USDA-CRGO Genetics Panel (1990-91); Editor, The Plant Journal, (1990-1994); Member, Plant Advisory Group, Cold Spring Harbor Laboratory (1990); Member, ASPP Executive Committee (1990-91); Member, NSF Biology Directors Advisory Committee (1992-1994); Member, AFRC IPSR Visiting Group (1993); Advisory Board, Noble Foundation (1993-97); Advisory Board, TIGR (1992-); Advisory Board, Molecular Genetics, Massachusetts General Hospital (1989-92); Member of Board, International Society for Plant Molecular Biology (1993-97); Associate Editor, Annual Review Plant Physiol. Plant Mol. Biol. (1993-97); Member, NRC Board on Agriculture (1994-96); Visiting committee, RSBS Australian National University (1995); Visiting committee, Swedish Foundation for Strategic Research (1995); Associate Editor, The Plant Cell (1995-2000); Editorial Board, Current Biology (1996-); Board of Reviewing Editors, Science (1996-); Editor, Current Opinion in Plant Science (1997-); Presidents Advisory Panel on Plant Biodiversity (1997-98); Editorial Board, Proc,. Natl. Acad. Sci, (1997-2000); Visiting committee ETH and University of Zurich (1997); Visiting Committee, Cornell Plant Biology (1998); Visiting Committee, Berkeley Plant Biology (1999); Scientific Advisory Board, The Wellcome Trust (1999-2001); Advisory Board, Danforth Center (1999-2001); Max-Planck-Institut für Moleculare Pflanzenphysiologie Fachbeirat (2000-); US-EU Consultative Forum on Biotechnology (2000). Alberta Heritage Foundation (2000-); Senior Editorial Committee, Science (2001-); John Innes Visiting Committee (2001); Cornell Biology Visiting Committee (2001-); University of Wisconsin Structural Biology Center Advisory Committee (2001-).

Stanford University Committeess (BIological Sciences):

Admissions Committee (1996-9)
Graduate committee (1996-8)
First Year Graduate Advising (1998-)

Patents:

Nucleic Acid Fragment encoding herbicide resistant plant acetolactate synthase, J.R. Bedbrook, R.S. Chaleff, S.C. Falco, B.J. Mazur, C.R. Somerville, N.S. Yadav. US Patent number 5,013,659, May 7, 1991

Nucleic Acid Fragment encoding herbicide resistant plant acetolactate synthase, J.R. Bedbrook, R.S. Chaleff, S.C. Falco, B.J. Mazur, C.R. Somerville, N.S. Yadav. US Patent number 5,141,870, August 25, 1992

Nucleic acid fragment encoding herbicide resistant plant acetolactate synthase. J.R. Bedbrook, R.S. Chaleff, S.C. Falco, B.J. Mazur, C.R. Somerville, N.S. Yadav. US Patent number 5,378,824 Jan 3, 1995

Nucleic acid fragment encoding herbicide resistant plant acetolactate synthase. J.R. Bedbrook, R.S. Chaleff, S.C. Falco, B.J. Mazur, C.R. Somerville, N.S. Yadav. US Patent number 5,605,011 Feb. 25, 1997

Production of petroselenic acid in transgenic plants, E. Cahoon, J. Ohlrogge, J. Shanklin, C.R. Somerville, US Patent number 05430134, Issued 7/4/1995
Process for producing polyhydroxybutyrate and related polyalkanoates in the plastids of higher plants. C.R. Somerville, C. Nawrath, Y. Poirier, U.S. Patent number 5,610,041, March 11, 1997

Transgenic plants producing polyhydroxyalkanoates, C.R. Somerville, Y. Poirier, D.E. Dennis, US Patent number 5,650,555, Issued 7/22/1997

Altered Linoleic and linolenic acid content in plants, C.R. Somerville, G. Kishore, T. Ruff, V. Arondel, S. Gibson, filed February 5, 1993

Use of plant fatty acyl hydroxylases to produce hydroxylated fatty acids and derivatives in plants. C.R. Somerville, F. van de Loo, US Patent number 5668292, Issued 9/16/1997

Use of plant fatty acyl hydroxylases to produce hydroxylated fatty acids and derivatives in plants. C.R. Somerville, F. van de Loo, US Patent number 5801026 issued 9/1/98

Fatty acyl CoA Reductase. C.R. Somerville and S. Reiser, US Patent number 6143538 issued 11/7/00

Production of hydroxylated fatty acids in genetically modified plants. C.R. Somerville, P. Broun, F. van de Loo, US Patent number #6,291,742 issued 9/18/2001

Plant Fatty Acid Hydroxylases. C.R. Somerville, P. Broun, F. van de Loo, US Patent number

#6310194 issued 9/30/2001

Structure and Expression of the biotin carboxylase subunit of heteromeric acetyl-CoA carboxylase. J. Ohlrogge, B. Shorrosh, D. Shintani, C. Somerville. 6218600 Issued April 17, 2001

Strong early seed-specific gene regulatory region. P. Broun, C. Somerville. US Patent number 5965793 issues 10/99.

Use of genes encoding xylan synthase to modify cell wall composition, C.R.. Somerville, S. Cutler, Filed April 1997.

Current Consulting

Scientific Advisory Board Mendel Biotechnology
Chairman of the Board, Mendel Biotechnoology
Founder, PGI (a startup focused on using phage integrase to make specific modifications of eukaryotic genomes)

Past Consulting

Dupont, Eli Lilly, Dow Elanco, Pioneer, Zeneca, Unilever, Keygene, Agridyne, Hoechst, Cold Spring Harbor, Massachusetts General Hospital, Monsanto

Invited Seminars:

Laboratorie Physico-Chemique de Foundation Rothschild, Paris; Du Pont Central Research Department, Wilmington, Delaware; University of Alberta, Edmonton, Alberta; York University, Toronto, Ontario; Du Pont Central Research Department, Wilmington, Delaware; Queens University, Kingston, Ontario; University of California, San Diego, California; Monsanto, St. Louis, Missouri; University of Toronto, Toronto, Ontario; Kettering Institute, Yellow Springs, Ohio; University of California, Davis, California; University of California, Berkeley, California; ARCO Research Institute, Dublin, California; University of Michigan, Ann Arbor, Michigan; Purdue University, W. Lafayette, Indiana; Shell Development Labs, Modesto, California; University of Colorado, Boulder, Colorado; University of Pennsylvania, Philadelphia, Pennsylvania; Washington University, St. Louis, Missouri; University of Utah, Salt Lake City, Utah; University of Chicago, Chicago, Illinois; Amoco Research Center, Chicago, Illinois; Rothamsted Experiment Station, Harpenden, England; Du Pont Central Research Department, Wilmington, Delaware; University of Washington, Seattle, Washington; Rockefeller University, New York, New York; Massachussetts General Hospital, Boston, Massachussetts; Cornell University, Ithaca, New York; University of Ghent, Ghent, Belgium;

University of California, Davis; MIT, Boston; University of Illinois, Urbana; Queens University, Kingston Ontario; Cold Spring Harbor Laboratory, Cold Spring Harbor, New York; Eli Lilley Research Dept, Indianapolis, Indiana; Case Western Reserve University, Cleveland, Ohio; Carnegie Mellon University, Pittsburgh, Pennsylvania; Dow Chemical Co, Midland, Michigan; Monsanto, St. Louis, Missouri; Washington State University, Pullman, Washington; Colorado State University, Fort Collins, Colorado; Scripps Research Institute, San Diego, California; Rockefeller University, New York; Louisiana State University, Baton Rouge, Louisiana; Cold Spring Harbor Laboratory, New York; McGill University, Montreal, Quebec; Iowa State University, Ames, Iowa; Pioneer HiBred Co., Des Moines, Iowa; Northern Illinois University, DeKalb, Illinois; University of Tokyo, Japan; Ajinomoto Co., Kawasaki, Japan; UCLA, Los Angeles CA; Oregon State University, Corvallis OR; University of Minnesota, Minneapolis MN; Brookhaven National Laboratories, Upton NY; University of Guelph, Guelph Ontario; Roche Institute, Nutley NJ; Ohio State University, Columbus OH; University of Saskatchewan, Saskatoon, Sask; Cornell University, Ithaca, NY; Monsanto, St Louis, MO; Cold Spring Harbor, NY; University of Wisconsin, Madison; University of Kansas, Manhattan, KS; University of Florida, Gainesville, FL; Harvard University, Boston, MA; Procter and Gamble, Cincinatti, OH; Calgene, Davis, CA; DNA PLant Technology, Oakland, CA; University of California, Berkeley, CA; Max-Planck-Institut für Zuchtungsforshung, Köln, Germany; Cold Spring Harbor Laboratory, New York; Monsanto Corporation, St. Louis, MO; John Innes Institute, Norwich, England; Cambridge University, Cambridge, England; Rockefeller University, New York, NY; University of Gerogia, Athens GA; MoGen International, Leiden, Netherlands; University of Kentucky, Lexington; University of British Columbia, Vancouver BC; UCLA, Los Angeles CA; Cold Spring Harbor Laboratory, Cold Spring Harbor, NY; Virginia Polytec, Blacksburg VA; University of Paris, Paris France; Salk Institute, San Diego, CA; Yale University, New Haven, CT; University of Alberta, Edmonton, Canada; Monsanto Corporation, St. Louis, MO; Friedrich Miescher Institute, Basel Switzerland; Cold Spring Harbor Laboratory, Cold Spring Harbor; University of California, San Diego; Laboratorium voor Genetica, Gent, Belgium; University of Nebraska, Lincoln; DuPont central Research, Wilmington DE; University of Arizona, Tucson AZ; Rockefeller University, New York; Pioneer Hybred International, Johnson City, IA; University of Iowa, Iowa City, IA; Cornell University, Ithaca, NY; Stanford UNiversity, Palo Alto, CA; University of California, Berkeley, CA; Oxford University, Oxford England; John Innes Institute, Norwich England; Max-Planck Institut, Koln, Germany; University of Freiburg, Freiburg Germany; University of Hamburg, Hamburg Germany; Hoechst, Frankfurt Germany; BASF, Mannheim Germany; University of Munich, Munich, Germany; ETH, Zurich; University of Calgary, Calgary Alberta; Purdue University; University of Oklahoma; Noble Foundation; Carlsberg Laboratory, Copenhagen; University of California, Davis; Rice University, Houston TX; Williams College; UC Santa Cruz, Santa Cruz CA; Washington University, St Louis MO; Texas A&M University, College Stn, TX; University of Tennesee, Knoxville TN; University of Lausanne, Lausanne Switzerland; Wageningen University, Wageningen, Netherlands; Max Planck Institute, Koln, Germany; University of Illinois; Penn State University; University of Nevada; University of Minnesota; Washington University; Colorado State University; KRIBB, Tejon, Korea

INVITED SYMPOSIA:

International Botanical Congress, Sydney, Australia (1981); Minnesota Spring Symposium, St. Paul, Minnesota (1982); Gordon Conference on Photosynthetic, Carbon Metabolism (1982); Miami Winter Symposium, Miami, Florida (1983); Plant Growth Regulator Society Meetings, E. Lansing, Michigan (1983); Gordon conference on Plant Molecular Biology, Andover, New Hamshire (1984); Genetics Society Meeting, Vancouver, B.C. (1984); UCLA Symposium, Keystone, Colorado (1985); US-Australia Workshop, Fraser Island, Australia (1985); Gordon Conference on CO2-fixation, New Hampshire (1985); American Chemical Society, Chicago, Illinois (1985); Royal Society of London, London, England (1986); Hoechst Molecular Biology Workshop, Graineau, W. Germany (1986); American Society of Plant Physiologists, Baton Rouge, Louisiana (1986); 7th International Congress in Plant Lipids, Davis, California (1986); Symposium on Genetic Engineering of Crops, Davis, California (1986); UCLA Symposium on Molecular and Cellular Biology, Part City, Utah (1987); Phytochem Society, Tampa, Florida (1987); FASEB, Copper Mountain, Colorado (1987); Lilly Symposium on Innovative Approaches to Agrichemical Research, Indianapolis, Indiana (1987); Toyobo Foundation Symposium on Plant Biotechnology, Nagaja, Japan (1987); National Institute for Basic Biology, Okazaki, Japan (1988); Purdue Symposium on Biotechnology, Purdue University, West Lafayette, IN (1988); Annual meeting American Society Plant Physiologists, Reno, NV (1988); International Congrees on Plant Lipids, Budapest, Hungary (1988); US-Japan Symposium on photosynthetic productivity, Honolulu Hawaii (1988); Gordon Conference on Temperature Stress in Plants, Oxnard CA (1989); American Oil Chemists Society, Cincinatti OH (1989); EMBO Symposium, Heidelberg, Germany (1989); Australian Biochemical Society Meeting, Brisbane Australia (1989); The Genetics and Molecular Biology of *Arabidopsis*, Bloomington, IN (1989); UCLA Symposium, Keystone, CO (1990); Ann. Mtg, American Society of Clinical Nutrition, Washington, DC (1990); Fourth International Arabidopsis Meeting, Vienna, Austria (1990); IX International Symposium on Plant Lipids, Wye College, England (1990); National Research Council Seed Oil Modification Workshop, Saskatoon, Canada (1990); Conference on Biotechnology for Safe and wholesome foods, Vlaardingen, Netherlands (1990); Symposium on Metabolic Compartmentation, Riverside, CA (1991); UCLA Symposium, Keystone, CO (1991); American Association for Advancement of Science Annual Meeting, Washington DC (1991); Canadian Genetics Society, Kingston, Ontario (1991); ICI-Harvard Frontiers of Science Symposium, Boston MA (1991); Penn State Symposium in Molecular Biology, College Station, PA (1991); Monod Conference on Membrane Flow, Roscoff, France (1991); Human Genome III, San Diego, CA (1991); Keystone Symposium on Crop Improvement via Biotechnology, Keystone CO (1992); 10th ISF World Congress & 83rd AOCS Annual Meeting, Toronto (1992); Gordon Conference on Plant Molecular Biology, Proctor Academy, NH (1992); Royal Society meeting on Transgenic plants and animals, London, England (1992); FEBS Meeting, Dublin, Ireland (1992); ACS International Symposium on Biotechnology, Washington, DC (1992); Foundation Ramon Areces Symposium "Biotechnology:the future today", Madrid, Spain (1992); EC-Bridge T-project, Copenhagen, Denmark (1992); US-Japan Workshop on

Molecular Biology of Plant Lipids, Kona HI (1992); Tel-Aviv Biotechnology Meeting, Tel-Aviv, Israel (1993); Royal Society Meeting on Transgenic Plants, London, England (1993); FEBS Meeting, Stockholm (1993); Recent Advances in Plant Molecular Biology, Kyoto Japan (1993); Annual Meeting of American Society of Plant Physiologists, Minneapolis, MN (1993); Annual Meeting of Canadian Society of Plant Molecular Biology, Toronto (1993); Genome V, Hilton Head, SC (1993); Chicago Symposium, Chicago IL (1993); Plant genome II, San Diego CA (1994); Federation of Canadian Biological Societies Annual Meeting, Montreal (1994); International Society for Plant Molecular Biology Congress, Amsterdam (1994); International Plant Lipid Congress, Paris (1994); Keystone meeting on Plant Cell Biology, Taos NM (1995); Glasgow University Symposium on Biochemical Genetics, Glasgow (1995); IAEA, Vienna, Austria (1995); Symposium on Plant genetic Engineering, Lexington KY (1995); National Academy of Sciences, Conference on resource sharing (1996); Workshop on Transgenic Plants, Tuskeege University, Tuskeege AL (1996); SEB Symposium on Plant Development, Dublin Ireland (1996); NATO Conference on Signals in Plant Development, Maratea, Italy (1997); National Academy of Sciences Symposium on Plant Genomes, Irvine CA (1997); National Plant Lipid Meeting, Lake Taho CA (1997); 17th International Congress of Biochemistry & Mol Biol, San Francisco (1997); Ninth International Genome Sequencing and Aanalysis Conference, Hilton Head SC (1997); International Society of Plant Molecular Biology Congress, Singapore (1997); International Prize in Biology Symposium, Kyoto (1997); Keystone meeting on Plant Cell Biology, Taos NM (1998); Swedish Foundation for Strategic Research Next Millenium Symposium (1998); American Society of Plant Physiologists, Madison WI (1998); Ohio State Biotechnology Symposium, Columbus OH (1998); National Academy meeting on the Future of Plant Biology, Lansing MI (1999); TIGR Genome meeting, Miami FL (1999); Biotechnology: Promises and Problems, The Hague (2000);DARPA Opportunities in AgBIotec Meeting (2000); AAAS Annual Meeting (2000); Thornton-Masa Lecture, Colorado State University (2000); Lemieux Lecture, University of Alberta (2000); International Biotechnology Congress, Berlin Germany (2000); Rothamstead Biomarket, Harpenden, England (2000); Plant development: Cell fate to Organ Formation, Capri, Italy (2000); American Chemical Society Annual meeting (2001); Kuhmo Symposium, Seoul Korea (2001); Annual meeting of American Botanical Society, Albuquerque NM

PUBLICATIONS

Books

Biochemistry and Molecular Biology of Membrane and Storage Lipids of Plants. N. Murata and C.R. Somerville, eds, American Soc. Plant Physiol., Rockville MD (1993)

Arabidopsis. E. Meyerowitz and C.R. Somerville, eds, Cold Spring Harbor Laboratory Press (1994)

Papers

Morgan, K., C.R. Somerville. Maximum entropy spectral analysis of monte carlo simulations of a closed finite human population. Can. Studies Populat. 3,1-17 (1976).

Somerville, C.R., A. Ahmed. *rel*-dependent methionine requirement in methionyl-tRNA synthetase mutants of *E. coli*. J. Mol. Biol. 111,77-81 (1977).

Somerville, C.R., A. Ahmed. Mutants of *E. coli* defective in the degradation of guanosine 5'-triphosphate, 3'-diphosphate (pppGpp). Molec. Gen. Genet. 169,315-323 (1979).

Somerville, C.R., W.L. Ogren. A phosphoglycolate phosphatase deficient mutant of *Arabidopsis*. Nature 280,833-836 (1979).

Somerville, C.R., W.L. Ogren. Photorespiration mutants of *Arabidopsis thaliana* deficient in serine:glyoxylate aminotransferase. Proc. Natl. Acad. Sci., USA 77,2684-2687 (1980).

Somerville, C.R., W.L. Ogren. Defective photosynthesis in mutants of *Arabidopsis* deficient in leaf glutamate synthase activity. Nature 286,257-259 (1980).

Somerville, C.R., S.C. Somerville, W.L. Ogren. Isolation of photosynthetically active protoplasts and chloroplasts from *Arabidopsis thaliana*. Plant Sci. Lett. 21,89-96 (1981).

Somerville, C.R., W.L. Ogren. Photorespiration deficient mutants of *Arabidopsis thaliana* lacking mitochrondrial serine transhydroxymethylase activity. Plant Physiol. 67,666-671 (1981).

Somerville, C.R., S.C. Somerville, W.L. Ogren. Genetic analysis of photorespiration. In: Proceedings of the Fifth International Congress on Photosynthesis (G. Akoyunoglou, ed.), Vol. VI, pp. 145-152 (1982).

Somerville, C.R., W.L. Ogren. Mutants of *Arabidopsis* deficient in glycine decarboxylase activity. Biochem. J. 202,373-380 (1982).

Somerville, C.R., W.L. Ogren. A mutant of *Arabidopsis* which lacks light activation of RuBP carboxylase. Plant Physiol. 70,381-387 (1982).

Somerville, C.R., W.L. Ogren. Genetic modification of photorespiration. Trends Biochem. Sci. 7,171-174 (1982).

Somerville, C.R., W.L. Ogren. Isolation of photorespiration mutants in *Arabidopsis thaliana*. In: Methods in Chloroplast Molecular Biology (M. Edelman, R.B. Hallick and N.H. Chua, eds.), Elsevier, pp. 129-138 (1982).

Somerville, C.R. Genetic modification of photorespiration. Whats New Plant Physiol., 13,29-32 (1982).

Somerville, S.C., C.R. Somerville. The effect of O_2 and CO_2 on photorespiratory flux determined from measurements of glycine accumulation in a mutant of *Arabidopsis*. J. Expt. Bot. 34,415-424 (1983).

Somerville, C.R., S.C. Somerville. Cloning and expression of the *Rhodospirillum rubrum* ribulose bisphosphate carboxylase gene in *E. coli*. Molec. Gen. Genet., 193,214-219 (1984).

Somerville, C., J. Fitchen, S. Somerville, L. McIntosh, F. Nargang. Enhancement of net photosynthesis by genetic manipulation of photorespiration and RuBP carboxylase/oxygenase. In: Advances in Gene Technology: Molecular Genetics of Plants and Animals, (F. Ahmad, K. Downey, J. Schultz and R. Voellmy, eds.) Academic Press, N.Y., pp. 295-309 (1983).

Ogren, W.L., C.R. Somerville, R.J. Spreitzer, M.H. Spalding. Strategies to improve photosynthesis by induced mutation. In: Selection in Mutation Breeding, (A. Micke, ed.) International Atomic Energy Agency, Vienna, pp. 59-66 (1984).
Nargang, F., L. McIntosh, C.R. Somerville. Nucleotide sequence of the ribulose bisphosphate carboxylase gene from *Rhodospirillum rubrum*. Molec. Gen. Genet. 193,220-224 (1984).

Ogren, W.L., C.R. Somerville, S.C. Somerville, R.J. Spreitzer, M.H. Spalding and D.B. Jordan. Genetic analysis of photosynthetic carbon pathways in higher plants. In: Advances in Photosynthesis Research, (C. Sybesma, ed.) Martinus NIjhoff, The Hague, Vol. 3, pp. 429-435 (1984).

McIntosh, L., J. Hirschberg, C.R. Somerville, J. Fitchen. Genetically altered chloroplast genes. In: Advances in Photosynthesis Research, (C. Sybesma, ed.) Martinus Nijhoff, The Hague, Vol. 4, pp. 483-490 (1984).

Somerville, C.R. The analysis of photosynthetic carbon dioxide fixation and photorespiration by mutant analysis. In: Oxford Surveys of Plant Molecular and Cell Biology, (B.J. Miflin, ed.), Oxford University Press, Vol. 1, pp. 102-133 (1984).

Somerville, C.R., S.C. Somerville. Les photosyntheses des plantes. La Recherche, 15,490-501 (1984).

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Somerville, S.C., C.R. Somerville. A mutant of *Arabidopsis* deficient in chloroplast

dicarboxylate transport is missing an envelope protein. Plant Sci. Lett. 37:217-220 (1985).

Browse, J., P. McCourt, C.R. Somerville. A mutant of *Arabidopsis* lacking a chloroplast-specific lipid. Science, 227,763-765 (1985).

Browse, J.A., C. Somerville, P. McCourt. Glycerolipid metabolism in leaves. New information from Arabidopsis mutants. In: Structure, Function and Metabolism of Plant Lipids. (P.A. Siegenthaler and W. Eichenberger, eds.), Elsevier, Amsterdam, pp. 101-104 (1984).

Somerville, C.R., L. McIntosh, M. Gurevitz, J. Fitchen. Cloning and expression in *E. coli.* of the large subunit of RuBP carboxylase/oxygenase. Methods in Enzymology, 118,419-433 (1986).

McIntosh, L., J.G. Williams, C. Somerville, M. Gurevitz. Genetic modification of photosynthesis. In: Molecular Form and Function of the Plant Genome. Fourth NATO Conference on Plant Mol. Biol., (L. van Vloten Dotten, ed.) Plenum Press, NY, pp. 335-346 (1985).

Caspar, T.C., S.C. Huber, C.R. Somerville. Effects on growth, photosynthesis and respiration in a starchless mutant of *Arabidopsis* deficient in chloroplast phosphoglucomutase. Plant Physiol. 79,11-17 (1985).

McCourt, P., J. Browse, J. Watson, C.J. Arntzen, C.R. Somerville. Analysis of photosynthetic antenna function in a mutant of *Arabidopsis thaliana* lacking *trans*-hexadecenoic acid. Plant Physiol. 78,853-858 (1985).

Artus, N.N., S.C. Somerville and C.R. Somerville. The biochemistry and cell biology of photorespiration. CRC Critical Reviews in Plant Sciences 4,121-147 (1986).
Gurevitz, M., C.R. Somerville, L. McIntosh. Pathway of assembly of ribulose bisphosphate carboxylase/oxygenase from *Anabaena* 7120 expressed in *E. coli*. Proc. Natl. Acad. Sci. USA. 82,6546-6550 (1985).

Estelle, M.E., J. Hanks, L. McIntosh, C.R. Somerville. Site-specific mutagenesis of ribulose 1,5-bisphoshate carboxylase/oxygenase: Evidence that carbamate formation at lys-191 is required for catalytic activity. J. Biol. Chem. 260,9523-9526 (1985).

Martinez, J., S.C. Somerville, C.R. Somerville. A possible case of position-effect variegation in *Arabidopsis thaliana*. In: Plant Genetics, UCLA Symp. Molec. Cell. Biol., (M. Freeling, ed.), Alan Liss Inc., N.Y., pp 828-829 (1985).

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Browse, J., N. Warwick, C.R. Somerville, C.R. Slack. Fluxes through the prokaryotic and eukaryotic pathways of lipid synthesis in the 16:3 plant *Arabidopsis thaliana*. Biochem. J. 235,25-31 (1986).

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Haughn, G.W. and C.R. Somerville. Selection for herbicide resistance at the whole plant level. In:Applications of Biotechnology to Agricultural Chemistry, (H. Le Baron, R.O. Mumma, R.C. Honeycutt, J.H. Duesing, eds.) American Chemical Society, pp. 98-108 (1987).

McCourt, P., C.R. Somerville. The use of mutants for metabolic studies in plants. In: The Biochemistry of Plants: A Comprehensive Treatise, (D. Davies, ed.), Academic Press, NY, Vol. 13, pp. 33-64 (1987).

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unsaturation on chloroplast ultrastructure and photosynthesis in a mutant of *Arabidopsis*. Plant Physiol. 84,353-361 (1987).

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Browse, J., Kunst, L., McCourt, P. and C.R. Somerville. Genetic manipulation of membrane lipid composition in *Arabidopsis*. In: Structure and Function of Plant Membranes, UCLA Symposium on Molecular and Cellular Biology, (Eds. H. Sze and C. Leaver), Alan R. Liss Inc., NY, (1987).

Haughn G., J. Smith, B. Mazur, C.R. Somerville. An *Arabidopsis* acetolactate synthase gene in tobacco confers resistance to sulfonylurea herbicides, Molec. Gen. Genet. 211,266-271 (1988).

Somerville, C.R., J. Browse. Genetic manipulation of the fatty acid composition of plant lipids. Adv. Phytochem. 22,19-45 (1988).

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Haughn, G.H., C.R. Somerville. Genetic control of morphogenesis in *Arabidopsis*. Devel. Genet. 9,73-89 (1988).

Finkelstein, R., M. Estelle, J. Martinez-Zapater, C.R. Somerville. *Arabidopsis* as a tool for the identification of genes involved in plant development. In: Plant Gene Research 5: Temporal and Spatial Regulation of Plant Genes, (eds. R. Goldberg, D.P. Venna), Springer-Verlag, N.Y., pp 1-25 (1988).

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Browse, J., C. R. Somerville, C. R. Slack. Changes in lipid composition during protoplast isolation. Plant Sci. 56,15-20 (1988)

Lin, T. P., T. Caspar, C. R. Somerville, J. Preiss. Isolation and characterization of a starchless mutant of *Arabidopsis thaliana* lacking ADP glucose pyrophosphorylase activity. Plant Physiol. 86,1131-1135 (1988).

Artus, N. N., C. R. Somerville. A mutant of *Arabidopsis* that exhibits chlorosis in air but not in atmospheres enriched in CO_2. Plant Physiol. 87,83-89 (1988).

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